

# Abstract

The invention concerns a process for optimizing the gene expression in cells. A first aspect concerns a process for changing the expression of a nucleic acid sequence which is present endogenously in a eukaryotic cell by introduction of a heterologous expression control sequence into the genome of the cell by means of homologous recombination as well as site-specific recombinase-mediated excision of inserted foreign DNA and its replacement by further heterologous expression control sequences or/and amplification genes. In addition the invention concerns the introduction of one or several nucleic acid sequences to which an activator protein or an activator protein complex binds e.g. a hypoxia-inducible factor (HIF), into the genome of a eukaryotic cell by homologous recombination in order to change the expression of a target gene. Furthermore the invention concerns a process for testing the influence of 5' or 3' non-coding nucleic acid fragments on the expression of a target gene by determining the expression of a reporter gene. In addition the invention concerns a process for providing a DHFR-negative eukaryotic cell containing a recombinase target sequence as well as the expression of a nucleic acid sequence inserted into the recombinase target sequence.

0920500-120123